formation in the presence of serum. Here it is present an alternative and specific paradigm for neural cell fate specification directly from ES cells. Neural colonies can develop from ES cells in serum-free conditions in the absence of EB formation, and many single ES cells can adopt a neural (nestin+) or neuronal (βIII-tubulin+) phenotype in the absence of exogenous growth factors. The derivation of neural cells from ES cells is preferrably carried out at relatively low cell densities in serum-free media. Low cell density as used herein refers to a cell culture density at which cell proliferation can occur with minimal and preferably no aggregation of ES cells or EB formation. Such densities are preferably about 50 or fewer cells/μl, most preferably less than 20 cells/μl, and even more preferred 10 or fewer cells/μl. It has been shown and a person skilled in the art would understand that the invention requires at least 1 cell to work, as such a cell density of greater than 0 is required. The present inventors have found (data not shown) that methods of the invention work significantly better in conditions where at about 10 or fewer cells/μl. Such a density results in a more homogenous cell culture i.e., primitive neural and neural cells as the case may be. The inventors have found that at this cell density, early mesodermal markers flk1 and brachyury are not expressed in the neurospheres derived clonally at lower densities from the novel single primitive neural stem cells of the invention. At higher densities, there is a greater likelihood that some, but not necessarily all that form by aggregation of ES cells that then differentiate to multiple tissue lineages and express the early mesodermal markers as noted above.

The experiments conducted by the inventors (data not shown) showed that single ES cells at such low densities will become neural stem cells. This is known because the single cells clonally proliferated to form spheres of 10,000 to 15,000 cells, all of which stained for an early ectodermal marker (nestin) and which do not express markers of other types of tissue like mesoderm, such as flk and brachyury. When a single sphere, clonally derived from a single primitive neural stem cell (the novel